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Differentiation of soft tissue benign and malignant peripheral nerve sheath tumors with magnetic resonance imaging

Chao-Shiang Li[a], Guo-Shu Huang[b], Hong-Da Wu[c], Wei-Tsung Chen[a], Li-Sun Shih[d], Jiunn-Ming Lii[a], Shyi-Jye Duh[a], Ran-Chou Chen[a,e], Hsing-Yang Tu[a], Wing P. Chan[e,f,*]

[a]*Department of Radiology, Taipei City Hospital–Renai Branch, Taipei, Taiwan, Republic of China*
[b]*Department of Radiology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, Republic of China*
[c]*Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan, Republic of China*
[d]*Department of Pathology, Taipei City Hospital–Renai Branch, Taipei, Taiwan, Republic of China*
[e]*Department of Radiology, School of Medicine, Taipei Medical University, Taipei, Taiwan, Republic of China*
[f]*Department of Radiology, Taipei Medical University–Wan Fang Hospital, Taipei, Taiwan, Republic of China*

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Abstract

Purpose: The objective of this study was to differentiate the magnetic resonance (MR) imaging appearance of benign peripheral nerve sheath tumors (PNSTs) from that of malignant PNSTs. **Materials and Methods:** Twenty-six patients who underwent MR imaging and had a histologic diagnosis of benign (schwannoma, n=16; neurofibroma, n=1) or malignant (n=9) PNST were retrospectively reviewed. The size, location, shape, margin, and signal intensities of the tumors on precontrast and gadolinium-enhanced MR imaging were analyzed. In each patient, the presence or absence of split fat, target, and fascicular signs was determined. **Results:** The mean size of the benign PNSTs (3.4 cm, S.D.=2.5 cm) was significantly smaller than that of the malignant tumors (8.2 cm, S.D.=3.1 cm) (P<.001). Seventeen (65.4%) of the 26 tumors were spindle shaped or ovoid (12 benign and 5 malignant tumors). Contiguity with specific nerves was identified in 15 (88.2%) of the 17 benign PNSTs but in none of the malignant tumors (P<.05). Well-defined margins were noted in all 17 benign PNSTs but in only 3 (33.3%) of the 9 malignant tumors (P<.001). Five (55.6%) of the 9 malignant PNSTs but none of the benign tumors showed signal intensity change in adjacent soft tissue (P<.05). There was no significant difference in signal intensity between the benign and malignant tumors on T_1-weighted, T_2-weighted, and contrast-enhanced MR images. The split fat and target signs were present more frequently in the benign PNSTs than in the malignant PNSTs (P<.05). **Conclusions:** Benign and malignant PNSTs are often spindle shaped. Recognition of contiguity with adjacent nerves, a well-defined margin, and the presence of the split fat sign may suggest benignity. Imaging features suggestive of malignancy can be a larger size and an infiltrative margin.

Keywords: Fascicular sign; Magnetic resonance (MR) imaging; Peripheral nerve sheath tumor; Split fat sign; Target sign

1. Introduction

Benign soft tissue neurogenic tumors include traumatic neuroma, Morton neuroma, neural fibrolipoma, nerve sheath ganglion, and benign peripheral nerve sheath tumor (PNST). Benign PNSTs are subdivided into two groups: schwannoma and neurofibroma. Neurogenic neoplasms represent 10%–12% of all benign soft tissue neoplasms [1,2]. Malignant soft tissue neurogenic neoplasms are called malignant PNSTs and account for 7%–8% of all malignant soft tissue neoplasms [3,4].

Soft tissue neurogenic neoplasms often reveal distinctive features: lesion location, clinical history, and radiological appearance. Neurogenic tumors can be diagnosed from their imaging appearances, including lesion shape and intrinsic

* Corresponding author. Department of Radiology, Taipei Medical University–Wan Fang Hospital, 111, Hsing-Long Road, Section 3, Taipei 116, Taiwan, Republic of China. Tel.: +886 2 2930 7930x1300; fax: +886 2 2931 6809.

E-mail address: wingchan@wanfang.gov.tw (W.P. Chan).

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imaging characteristics [5]. A better prognosis can be achieved if malignant PNSTs are diagnosed at an early stage [6].

The aim of this study was to differentiate the magnetic resonance (MR) imaging appearance of benign PNSTs from that of malignant PNSTs.

2. Materials and methods

2.1. Patients

This study was designed as a retrospective review of medical records and MR images, and therefore institutional review board approval was waived. This study recruited 26 patients who underwent MR imaging and who each had a histologically proven soft tissue PNST. Of the patients, 19 were men and 7 were women (mean±S.D. age=47.0±16.6 years, range=20–82 years). All cases were searched from the histologic database of four institutions. All 26 patients complained of palpable masses and received surgical resection. Twenty patients had imaging data at the time of their initial clinical presentation, whereas the rest of the patients with malignant PNSTs underwent MR imaging after surgery on recurrence. For all tumors, the histologic diagnosis revealed a schwannoma in 16 cases, a neurofibroma in 1 case, and a malignant PNST in 9 cases.

2.2. Magnetic resonance imaging

Magnetic resonance imaging was performed with 1.5-T MR scanners (Philips Gyroscan ACS-NT, Best, The Netherlands, for 7 patients; Horizon LX, General Electric, Milwaukee, WI, USA, for 5 patients; Vista, Picker, Cleveland, OH, USA, for 8 patients; Siemens Magnetom Vision, Erlangen, Germany, for 6 patients). Axial and sagittal and/or coronal images were obtained. Imaging planes, pulse sequences, section thickness, field of view, matrix size, and number of signal averages for data acquisition were determined according to the area being examined. Most imaging protocols included spin-echo T_1-weighted imaging (repetition time=400–550 ms, echo time=12–20 ms) without fat saturation and turbo spin-echo or fast spin-echo T_2-weighted imaging (repetition time=2400–3350 ms, echo time=70–100 ms, turbo spin-echo factor=23) with and that without fat saturation. Gadolinium-enhanced images were obtained for 19 patients (9 with schwannoma, 1 with neurofibroma, and 9 with malignant PNST) after a manual intravenous injection of gadopentetate dimeglumine (0.1 mmol/kg of body weight; Magnevist, Schering, Berlin, Germany). Axial and sagittal and/or coronal images were also obtained. For each patient, fat-saturated and non-fat-saturated pulse sequences were performed in at least one plane of the MR images.

2.3. Imaging analysis

All MR images were interpreted by two radiologists independently, and disagreement in interpretation was solved

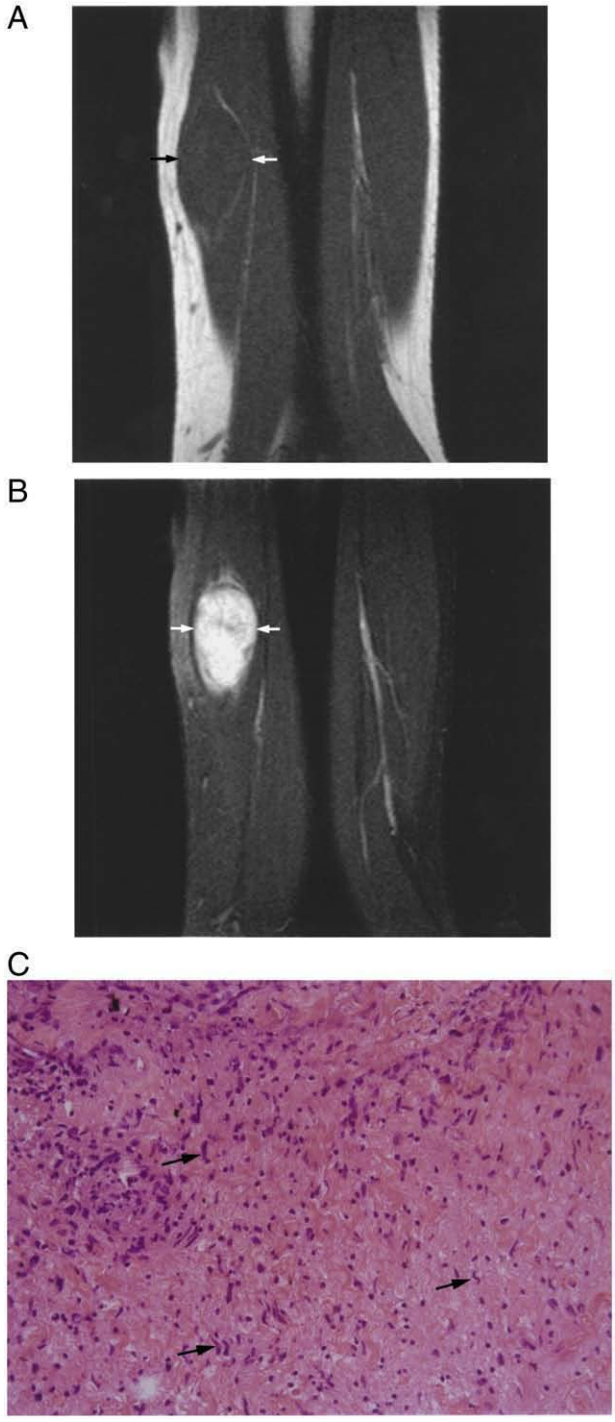

Fig. 1. Images of a neurofibroma of the ulnar nerve of the left arm in a 58-year-old man who had a long-standing palpable mass. (A) Coronal T_1-weighted MR image (400/12) showing a spindle-shaped mass (arrows) with isointensity to the adjacent muscle. (B) Coronal fat-saturated and T_1-weighted gadolinium-enhanced MR image (720/14) showing heterogeneous enhancement of the mass (arrows). (C) Photomicrograph (hematoxylin–eosin stain, original magnification ×200) showing that the tumor was composed of bland-appearing spindle cells with wavy nuclei (arrows) in loose fibromyxoid stroma.

by consensus in a joint meeting. The location of the tumor was described with emphasis on any contiguity with a specific peripheral nerve. The shape of the tumor was determined as to whether it was spindle shaped or ovoid. The signal intensities of the tumor on T_1-weighted, T_2-weighted, and gadolinium-enhanced images were recorded. The signal intensity of a tumor was compared with that of the adjacent skeletal muscles on T_1-weighted images, and subcutaneous fat was analyzed on T_2

(P<.001, Student's t test). A spindle or ovoid shape was noted in 12 (70.6%) of the 17 benign PNSTs (Fig. 1) and in 5 (55.6%) of the 9 malignant tumors (P=.67, Fisher's exact test). Four cases of schwannoma exhibited multilobular appearances, ranging from two to six lobules oriented linearly and contiguous with each other (Fig. 2).

Contiguity with specific nerves of the tumors was identified in 15 (88.2%) of the 17 benign PNSTs: 5 with the median nerve, 5 with the ulnar nerve, 2 with the radial nerve, as well as 1 each with the sciatic nerve, brachial plexus, and dorsal antebrachial cutaneous nerve. On the contrary, contiguity with specific nerves could not be identified in the 9 malignant PNSTs (P<.05).

Tumors with well-defined margins were noted in all 17 benign PNSTs and in 3 (33.3%) of the 9 malignant PNSTs (P<.001); the remaining 6 (66.7%) malignant PNSTs depicted ill-defined margins (Fig. 3). Five (55.6%) of the 9 malignant PNSTs showed signal intensity changes (high signals to adjacent soft tissue on T_2-weighted pulse sequences), whereas none of the benign PNSTs showed abnormal MR signals to adjacent soft tissue (P<.05). None of the tumors had invasion to adjacent muscular or bony structures regardless of benignity or malignancy.

All 26 tumors exhibited isointensity to adjacent muscles on T_1-weighted images. On T_2-weighted images, 14 (82.4%) of the 17 benign PNSTs and 7 (77.8%) of the 9 malignant PNSTs were hyperintense; the other 3 (17.6%) benign PNSTs and 2 (22.2%) malignant PNSTs were hypointense with heterogeneity of MR signals. On gadolinium-enhanced images, the benign PNSTs (n=10) showed faint to strong enhancement, with homogeneous enhancement in 6 (60.0%) tumors and heterogeneous enhancement in 4 (40.0%). The 9 malignant PNSTs also showed homogeneous (n=3, 33.3%) or heterogeneous (n=6, 66.7%) hyperintensity. There was no difference between the benign and malignant PNSTs with respect to MR signals (P=1.0) and enhancing patterns (P=.37).

The split fat sign was present in 13 (76.5%) of the 17 benign PNSTs and in 3 (33.3%) of the 9 malignant PNSTs (P=.046). The target sign was noted in 8 (47.1%) benign PNSTs (Fig. 2C and D) but was absent in all 9 malignant PNSTs (P<.05). The fascicular sign was shown in 6 (35.3%) benign PNSTs (5 schwannomas and 1 neurofibroma) (Fig. 4B and C) but was absent in all 9 malignant PNSTs (P=.063).

4. Discussion

Peripheral nerve sheath tumors are soft tissue neoplasms derived from Schwann cells. As with other soft tissue

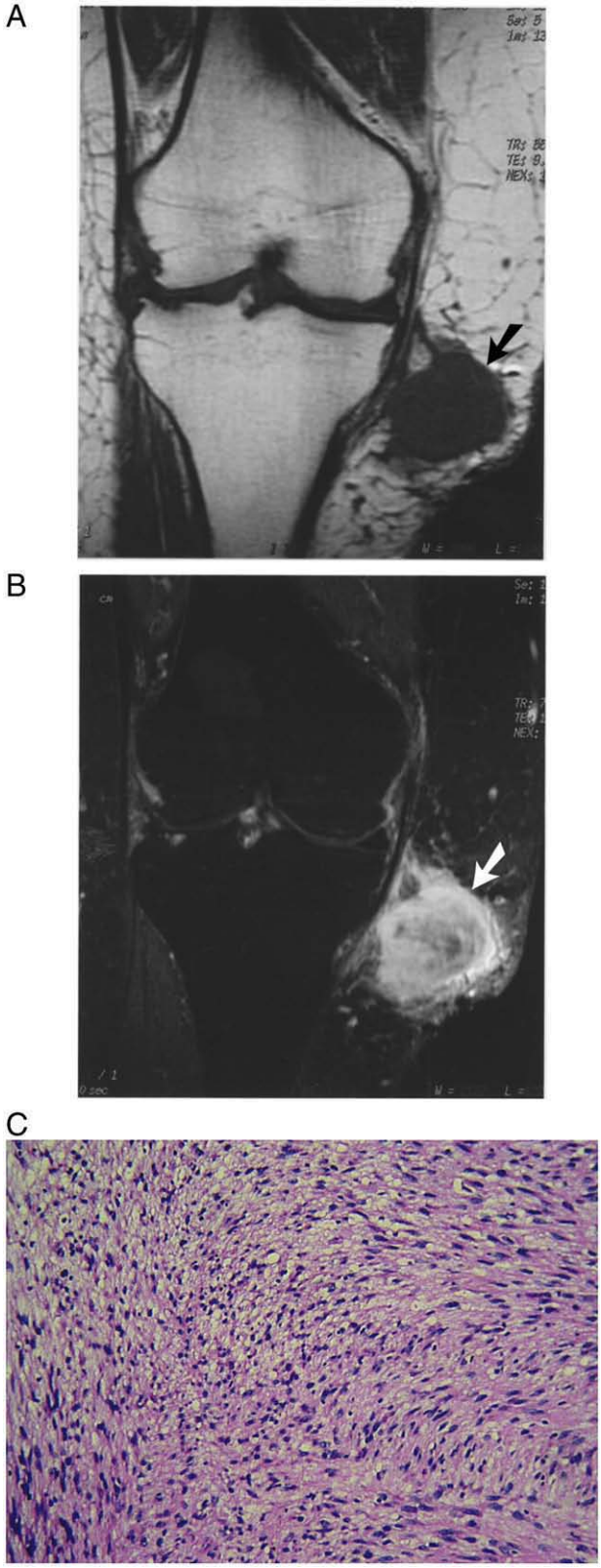

Fig. 3. Images of a malignant PNST involving the subcutis of the right knee in a 65-year-old woman. (A) Coronal T_1-weighted MR image (550/9.9) showing that the mass (arrow) has a partially ill-defined margin and is isointense to adjacent muscles. (B) Coronal fat-saturated and proton density-weighted MR image (2800/20.5) showing that the mass (arrow) is inhomogeneous and hyperintense with abnormal high signal intensity to adjacent soft tissue. (C) Photomicrograph (hematoxylin–eosin stain, original magnification ×200) showing a cellular tumor composed of interlacing fascicles of neoplastic spindle cells with plump and hyperchromatic nuclei. Immunostaining for S-100 was positive (not shown), supporting the tumor's nerve sheath origin.

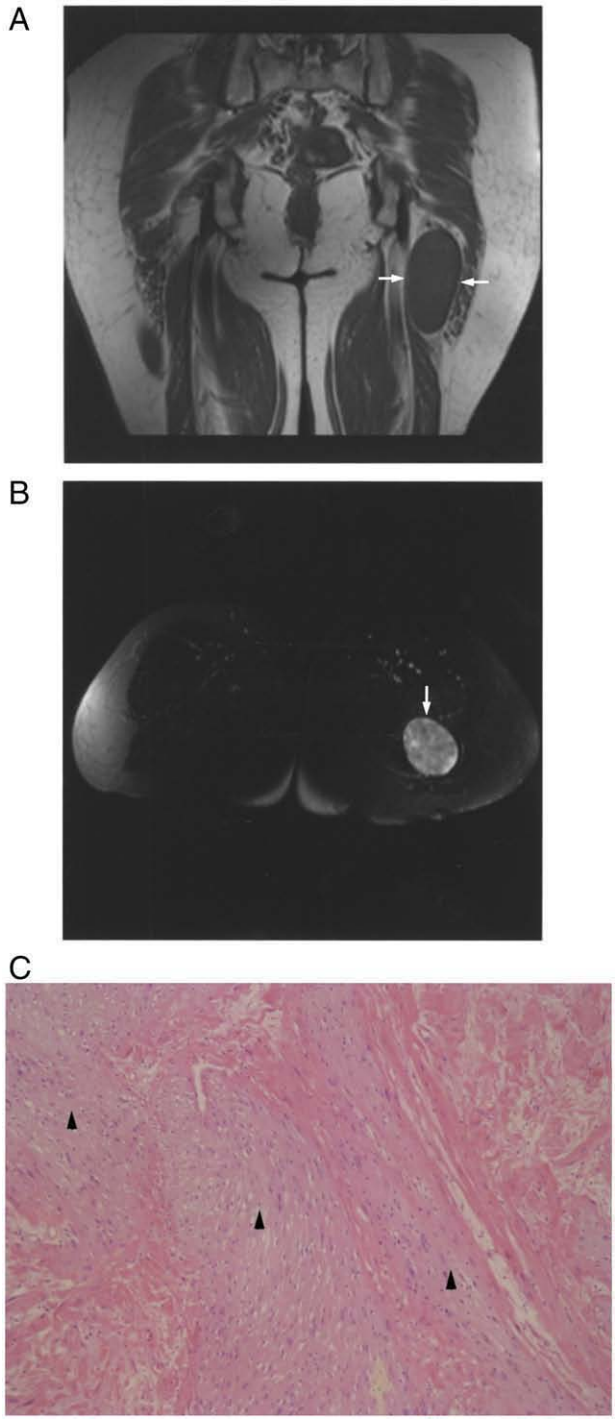

Fig. 4. Images of a neurilemoma involving the sciatic nerve in the left gluteal region in a 55-year-old woman. (A) Coronal T_1-weighted MR image (472/20) showing a spindle-shaped mass (arrows) surrounded by fat, representing the split fat sign. (B) Axial fat-saturated and T_2-weighted MR image (2485/70) showing a hyperintense mass (arrow) with multiple small hypointense fascicle-like structures in the mass, representing the fascicular sign. (C) Photomicrograph (hematoxylin–eosin stain, original magnification ×100) showing a fascicular appearance of cellular parts (arrowheads).

neoplasms, these lesions are more easily characterized with advanced imaging techniques [8]. Magnetic resonance imaging is superior to ultrasound and computed tomography in demonstrating features of soft tissue tumors because of its excellent tissue contrast and multiplanar capability; in addition, MR imaging has become the method of choice for evaluating the anatomical location, contour, and relationship of a nerve sheath tumor with adjacent neural, vascular, and muscular structures [9].

Schwannomas and neurofibromas are the two most common types of a PNST, but they are difficult to be distinguished with imaging [10]. Jee et al. [11] reported that MR imaging features were helpful in differentiating neurofibromas from schwannomas but that no single finding or combination of findings allowed for a definitive differentiation.

In our study, the most important MR imaging features to suggest the diagnosis of a PNST were spindle or ovoid shape and contiguity with a specific nerve. A spindle or ovoid shape was observed in 66% of the tumors in our study. The morphology represents a tumor located in a nerve distribution and connected to an entering and exiting tubular nerve [5]. Benign and malignant PNSTs may similarly show this characteristic morphology. Contiguity with a specific nerve was also observed in 58% of the tumors in our study, and all were benign. Cerofolini et al. [12] reported this finding in 94% of their 17 patients who had benign PNSTs. The relationship between the tumor and a specific nerve was usually easy to be detected in lesions affecting large and deep nerves. In contrast, in cases with a subcutaneous location, a muscular nerve branch origin, and an extensive tumor, the nerve of origin was often difficult to be identified. We suggest that contiguity with a specific nerve may support the diagnosis of a benign PNST rather than a malignant one.

The signal intensities of PNSTs on MR imaging were usually isointense to adjacent muscles on T_1-weighted images and hyperintense on T_2-weighted images. A few PNSTs were relatively hypointense with heterogeneity on T_2-weighted images, and the appearance was possibly a result of the different compositions of the tumors. Tumors with a high myxoid or water content would have hyperintensity on T_2-weighted images, but tumors with more cellular components might be relatively hypointense [13]. In our study, benign and malignant PNSTs shared the same MR signal characteristics and showed various enhancements on gadolinium-enhanced MR imaging. The signal intensity of the tumor was not a reliable indicator of differentiation between benign and malignant PNSTs in our study.

In our study, all benign PNSTs had well-defined margins. However, 67% of the malignant PNSTs had partially ill-defined margins and the rest had an abnormal signal intensity to adjacent soft tissue. These two features had been considered by other authors as manifestations of aggressive soft tissue lesions, including malignant tumors and infectious or inflammatory lesions [14].

A rim of fat (the split fat sign) was present in 62% of the PNSTs in our study, including 13 benign and 3 malignant

tumors. Because the neurovascular bundle is normally surrounded by fat, masses arising at this site maintain a rim of fat about them as they slowly enlarge. This is not a specific sign for PNST but is suggestive of an intermuscular lesion about the neurovascular bundle [5]. The split fat sign is more common in benign PNSTs and lesions of large nerves [5,15,16]. A malignant PNST less frequently shows the split fat sign, reflecting its more infiltrative growth pattern [5].

The MR imaging target sign consists of low to intermediate signal intensity centrally with a ring of high signal intensity peripherally on T_2-weighted images. This finding corresponds pathologically to a more cellular Antoni type A region centrally and a more myxoid Antoni type B region peripherally [5,13]. A positive target sign was demonstrated in 47% of the benign tumors in our study, and all of them were schwannomas. The sign was not present in malignant PNSTs in our study. Suh et al. [13] described this sign in 70% of 10 cases of neurofibroma. Although the target sign has always been described as being nearly pathognomonic for neurofibromas, it can be seen in schwannomas and less frequently in malignant PNSTs [5]. We suggest that the target sign is helpful in differentiating between benign and malignant PNSTs.

In the fully developed nerve, a layer of connective tissue or an epineurium surrounds the entire nerve trunk. Bundles of nerve fibers are surrounded by a perineurium [2,5]. This gross appearance can be recognized on MR imaging and has been described as a fascicular appearance [15]. The fascicular sign can be seen in neurogenic neoplasms and corresponds to the fascicular bundles seen on pathology in neurogenic neoplasms, particularly in more differentiated benign PNSTs [5]. This manifestation was also observed in our study: 35% of the benign PNSTs but none of the malignant PNSTs showed the fascicular sign.

In our experience, the presence of the target and fascicular signs on MR imaging may not be appreciated because of improper instrument window and level settings that can obscure the hypointensity in the central area of the tumor. Use of wide window settings to allow for characterization of the internal architecture of a mass had been recommended by other authors [7] to increase the sensitivity of the target and fascicular signs.

In our study, we also noted four cases of schwannoma that had a multilobular appearance along a nerve. The four patients involved had no clinical evidence of neurofibromatosis. A bilobular appearance may be explained by the origin of the lesion at the level of nerve bifurcation [15]. However, the trilobular or multilobular appearance of PNSTs has not been discussed previously in the English literature, and the mechanism of this morphology is not clear. We suggest that a multilobular appearance of a soft tissue tumor may also be a feature of PNST.

The variety of patients who underwent MR imaging with four scanners was a limitation of our study. Some variations in imaging protocols existed, but these protocols were appropriate for analysis.

In conclusion, most soft tissue PNSTs show nonspecific MR appearances; however, recognition of the spindle or ovoid shape of the tumor and contiguity of the tumor and adjacent nerves may suggest the diagnosis. Differentiation of benign from malignant PNSTs is often difficult. Imaging features suggestive of malignancy can be a larger size, an ill-defined margin, and MR signal changes in adjacent soft tissue. On the other hand, imaging features of benign PNSTs include a smaller size, recognition of contiguous nerves, a well-defined margin, and the presence of the split fat and target signs. The fascicular sign is suggestive of a benign PNST.

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